OIPE IAP97 DEC 12 2006 PATENT & TRADEMARK OFFICE

IFW

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Peter BAETS et al. | Group Art Unit: 1753

Application No.: 10/693,922 | Examiner: A. PHASGE

Filed: October 28, 2003 | Docket No.: 117622

For: METHOD OF SEPARATING MULTIVALENT IONS AND LACTATE IONS FROM A FERMENTATION BROTH

CLAIM FOR PRIORITY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The benefit of the filing date of the following prior foreign application filed in the following foreign country is hereby requested for the above-identified patent application and the priority provided in 35 U.S.C. §119 is hereby claimed:

European Patent Application No. 02079493.3 filed October 28, 2002

In support of this claim, a certified copy of said original foreign application:

☒ is filed herewith.

It is requested that the file of this application be marked to indicate that the requirements of 35 U.S.C. §119 have been fulfilled and that the Patent and Trademark Office kindly acknowledge receipt of this document.

Respectfully submitted,

Ryan C. Cady

James A. Oliff
Registration No. 27,075

Ryan C. Cady
Registration No. 56,762

JAO:RCC/amw

Date: December 12, 2006

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE
AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our
Deposit Account No. 15-0461

Europäisches Patentamt | European Patent Office | Office européen des brevets

Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

02079493.9

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

Anmeldung Nr:
Application no.: 02079493.9
Demande no:

Anmeldetag:
Date of filing: 28.10.02
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

Purac Biochem N.V.
Arkelsedijk 46
4206 AC Gorinchem
PAYS-BAS

Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se referer à la description.)

Method of separating multivalent ions and lactate ions from a fermentation broth

In Anspruch genommene Prioriät(en) / Priority(ies) claimed /Priorité(s) revendiquée(s)
Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

B01D61/00

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR

EP 5093-Be

METHOD OF SEPARATING MULTIVALENT IONS AND LACTATE IONS FROM A FERMENTATION BROTH

The invention pertains to a method of separating multivalent ions and lactate ions from a fermentation broth comprising a multivalent ion lactate salt by using an electrodialysis or electrolysis apparatus. The invention further relates to an electrodialysis or electrolysis apparatus for separating a fermentation broth into a residual stream comprising multivalent ions and lactate ions.

Methods of separating monovalent ions and lactate ions from a fermentation broth comprising a monovalent ion lactate salt by using an electrodialysis or electrolysis apparatus are well known in the art. In US 5,002,881 a process is described for the fermentative preparation of lactic acid by fermenting a culture of Bacillus in an aqueous solution comprising sodium, potassium, or ammonium ions, subjecting the reaction mixture to ultrafiltration and subjecting the permeate to an electrodialysis wherein bipolar membranes are used.

Preferred lactic salts are sodium, potassium, and ammonium lactates, as was also disclosed in US 5,681,728, which further makes use of an electrodialysis apparatus to purify sodium, potassium, or ammonium lactate from a complex feed stream.

Specific electrodialysis processes and apparatus for converting sodium and ammonium lactate tot lactic acid anion have been described in US 6,221,225. In this patent a stack of electrodialysis cells is used to form a multiplicity of compartments for separation.

As above, exclusively sodium, potassium, or ammonium salts of lactic acid are used, because these are water-soluble and it is important to prevent fouling of the membrane. Fouling would frustrate the electrodialysis process, and necessitates regular cleaning of the equipment and therefore interrupting the process.

For economical reasons this is an unwanted situation. Therefore, it is commonly accepted that multivalent ions should be prevented in the electrodialysis process. However, the neutralization in the fermentation process is preferably performed with multivalent ions, not with sodium, potassium, or ammonium hydroxide. In WO 98/28433 a method is proposed to prevent scaling on purifying divalent salts of lactic acid as obtained after the fermentation process. The permeate of an ultrafiltration process, for that reason, is treated in an ion exchange unit to bind calcium and magnesium ions, and other multivalent ions like iron ions, if present. This method prevents the precipitation of salts, such as calcium phosphate that may lead to irreversible scaling of the membrane. However, this method requires an extra exchange step and makes the end product unnecessary expensive.

It is therefore an objective of the present invention to provide a method of directly separating multivalent ions and lactate ions from a fermentation broth comprising a multivalent ion lactate salt by using an electrodialysis or electrolysis apparatus, without the need of an extra step of exchanging divalent ions for monovalent ions.

The present invention provides in a method satisfying the above conditions by performing the method comprising the steps of introducing the broth wherein the multivalent ion concentration is at least 0.1 mole/l, the lactate ion concentration is less than 300 g/l, and less than 10 mole% of the lactate ion are other negatively charged ions, into a first compartment of the electrodialysis or electrolysis apparatus, which compartment is limited by an anion-selective or non-selective membrane and a cathode, and wherein the multivalent ion is converted to obtain a residual stream comprising the hydroxide of the multivalent ion, and the lactate ion is transported through the anion-selective or non-selective membrane into a second compartment limited by the anion-selective or non-selective membrane and an anode, after which the lactate ion is neutralized to lactic acid.

The method according to the invention preferably makes use of a broth containing per equivalent of lactate ion at least 0.1 equivalent of the multivalent ion, and more preferably at least 0.3

equivalents of the multivalent ion. Preferably, the multivalent ion concentration in the broth is 0.1 - 1.5 mole/l. The broth is obtained by the common procedure such as by fermentation of a carbohydrate (for instance glucose, starch, sucrose, and the like).

The multivalent ion is preferably a multivalent metal ion selected from magnesium, calcium, zinc, iron, and aluminum, and mixtures thereof.

In another preferred embodiment according to the invention the fermentation broth comprises microorganisms. It is suitable to recycle the residual stream to the fermentation broth. It is also advantageous when the hydroxide of the multivalent ion is at least partially deposited.

In a particularly preferred embodiment according to the invention the membrane is an anion-selective membrane.

The invention further relates to an apparatus for performing the above methods. Thus according to the invention there is provided an electrodialysis or electrolysis apparatus for separating a fermentation broth into a residual stream comprising multivalent ions and lactate ions, comprising a first compartment which is limited by an anion-selective or non-selective membrane, preferably an anion-selective membrane, and a cathode, which further comprises means for introducing the fermentation broth, and a second compartment limited by the anion-selective or non-selective membrane and an anode, which further comprises means for removing lactic acid, and optionally means to recycle the residual stream of the first compartment to the fermentation broth.

The above electrodialysis or electrolysis apparatus may contain a first compartment further comprising a second membrane being an anion-selective membrane, a non-selective membrane, or a bipolar membrane having its cation-selective side directed to the cathode.

In another embodiment according to the invention the electrodialysis or electrolysis apparatus comprises a first compartment with alternating anion-selective or non-selective membranes, and bipolar membranes having their cation-selective sides directed to the cathode. Most preferred these extra membranes are of the anion-selective type.

The invention is illustrated by the following figures.

Fig. 1 is a schematic view of an electrodialysis or electrolysis apparatus in its simplest form, i.e. containing an anode and a cathode and an anion-selective or non-selective membrane in between.

Fig. 2 is a schematic view of an electrodialysis or electrolysis apparatus comprising a second anion-selective membrane.

Fig. 3 is a schematic view of an electrodialysis or electrolysis apparatus with alternating anion-selective and bipolar membranes.

Fig. 4 is a scheme showing the electrodialysis or electrolysis apparatus according to Fig. 1, a product container (P), and the fermentor (F) for converting the sugar to a multivalent salt of lactic acid.

In Fig. 1 an electrodialysis or electrolysis cell is shown with an anode (a) indicated with charge + and a cathode (c) indicated with charge -. Between the anode and cathode a membrane (A) is placed which can be an anion-selective or non-selective membrane. Examples of anion-selective membranes are found in handbooks (e.g. K. Scott, Handbook of industrial membranes, 2nd edition, 1998, ISBN 1856172333, p. 257-269) and comprise (a) heterogeneous ion exchange membranes, which consist of fine colloidal ion-exchange particles embedded in a suitable binder (phenolic resins, PVC, etc.), or (b) homogeneous membranes, which consist of a polymer film with functional groups (often a quaternary ammonium group NR_3^+), or (c) fluorocarbon membranes with functional groups (often a quaternary ammonium group NR_3^+) and mixtures thereof. Examples of non-selective membranes are described in the literature (e.g. Perry's Chemical Engineers' Handbook, sixth edition, R.H. Perry and D. Green, 17-14/17-34 and Kirk-Othmer's Encyclopedia of Chemical Technology, Third Edition, Vol.8, p.698, Chapter Diaphragms), and comprise materials and modified materials with a well selected porosity of cellulose, ceramics, rubbers, silicates, boro-silicates, asbestos, and polymers such as silicones, nylon, polyethylene terephthalate, teflon, polystyrene, polyethylene, polypropylene, polybutadiene, polyamide, polyfuranes, polyacrylonitrile, polysulfones, PVC's, polycarbonate, polyvinyl

derivatives, and mixtures thereof. These materials may be available in various physical forms including mats, sheets, films, sintered forms, and woven or non-woven cloths.

Thus the cell comprises a first compartment (I), which compartment is limited by the anion-selective or non-selective membrane (A) and the cathode (c). In this example calcium lactate is placed in compartment (I), after which on applying current in the cell the calcium ions form calcium hydroxide that may at least partially deposit in compartment (I) and leaves this compartment either as a solution of ions or as a slurry with solid hydroxide, whereas the lactate anion passes through the membrane (A) and leaves the second compartment (II), which compartment is limited by the anion-selective or non-selective membrane (A) and the anode (a), as lactic acid (HL). The figure further shows the electrolytic reactions that occur, wherein hydrogen is formed at the cathode and oxygen at the anode.

In Fig. 2 an embodiment is shown according to claim 10, wherein the first compartment further comprises a second anion-selective or non-selective membrane (A), dividing compartment (I) in two parts, i.e. Ia and Ib. The electrolysis processes occurring in this cell are the same as shown in Fig. 1, but the additional anion-selective or non-selective membrane acts as an extra protecting membrane, further preventing fouling of the multivalent ion at the cathode and/or anode. According to this embodiment the multivalent salt (in this particular case calcium) of lactic acid is introduced in section Ib of compartment I, keeping the calcium physically away from both the anode and cathode.

In Fig. 3 an embodiment is shown according to claim 11, wherein a stack of three cell combinations has been formed. According to this embodiment, anion-selective or non-selective membranes (A), preferably anion-selective membranes, alternate with bipolar membranes (BP) having their cation-selective sides directed to the cathode. The compartments indicated with Ca^{++} are compartments wherein the multivalent salt of lactic acid is introduced. The electrodialysis process is in principle the same as that of Figs. 1 and 2, but lactic acid (HL) leaves the cell in three different

product streams. It is clear that according to this principle any stack with any number of cells can be made.

The invention is further illustrated with the following non-limitative examples.

Example 1

A cell according to Fig. 1 comprises an ACM™ membrane (ex Tokuyama), a titanium cathode and a DSA anode, the distance of the cathode and anode to the membrane being both 8 mm. The membrane surface is 10*10 cm^2 and the volume of each of the compartments is 80 cm^3. The current is adjusted to 40 mA/cm^2 (4 A). The liquid yield is 117 l/h at the anolyte and 105 l/h at the catholyte at a working temperature of 55°C. The catholyte volume is 2 l, comprising a 12 wt.% calcium lactate solution, and the anolyte volume is 0.5 l, comprising a 5 wt.% lactic acid solution initially. The pH of the catholyte during the experiment is kept below 10 by addition of acid (90 wt.% lactic acid).

The voltage could be kept between 15 and 19 V to maintain a current of 4 A during this experiment (5 h), during which time the concentration of lactic acid increases from 5 wt.% to 17.4 wt.%. The electrodes remained free from scaling.

Example 2

The experiment of Example 1 was repeated, keeping the conditions the same with the exception that the liquid yield is 114 l/h at the anolyte and 120 l/h at the catholyte at a working temperature of 60°C.

Contrary to Example 1 no acid was added during the experiment. The voltage was kept between 15.3 and 18.6 V to maintain a current of 4 A during this experiment (122 min), during which time the pH increased to 12.43. The catholyte became white, due to the formation of milk of lime (a calcium hydroxide slurry), but the electrodes remained free from scaling. The lactic acid concentration increased from 5 wt.% to 11 wt.% during the experiment.

Example 3

An electrolysis cell according to Fig. 1, using a non-selective porous cellulose acetate membrane (pore diameter 0.8 μm; ex Sartorius), was used in combination with a feed container, and a fermentor for converting the feed to a multivalent salt of lactic

acid, as depicted in Fig. 4. The fermentation of sucrose to lactic acid was started by addition of milk of lime to control the pH at 6.4 and after 20 h, which time is necessary to obtain a sufficient amount of conductive salt, the addition of milk of lime was stopped and the electrolysis was started under pH control. The pH of the fermentation was kept at 6.4. The lactate anion was transported from fermentor (F) to feed container (P) (see Fig. 4) through the membrane by applying current. The pH in P (the 12 wt.% calcium lactate solution at 54°C) decreased during this process (see Table), showing that lactic acid was separated from the fermentation liquid.

Table

Time (min)	pH (calcium lactate)	I (A)	V
0	5.61	0.5	2.35
90	4.86	0.67	2.82
180	4.55	0.78	2.99
260	4.40	0.67	2.89
310	4.34	0.72	2.96

Claims:

1. A method of separating multivalent ions and lactate ions from a fermentation broth comprising a multivalent ion lactate salt by using an electrodialysis or electrolysis apparatus, comprising the steps of introducing the broth wherein the multivalent ion concentration is at least 0.1 mole/l, the lactate ion concentration is less than 300 g/l, and less than 10 mole% of the lactate ion are other negatively charged ions, into a first compartment of the electrodialysis or electrolysis apparatus, which compartment is limited by an anion-selective or non-selective membrane and a cathode, and wherein the multivalent ion is converted to obtain a residual stream comprising the hydroxide of the multivalent ion, and the lactate ion is transported through the anion-selective or non-selective membrane into a second compartment limited by the anion-selective or non-selective membrane and an anode, after which the lactate ion is neutralized to lactic acid.
2. The method according to claim 1 wherein the broth contains per equivalent of lactate ion at least 0.1 equivalent of the multivalent ion, and preferably at least 0.3 equivalents of the multivalent ion.
3. The method according to claims 1 or 2 wherein the multivalent ion concentration in the broth is 0.1 - 1.5 mole/l.
4. The method according to any one of claims 1-3 wherein the multivalent ion is a multivalent metal ion selected from magnesium, calcium, zinc, iron, aluminum, and mixtures thereof.
5. The method according to any one of claims 1-4 wherein the fermentation broth comprises microorganisms.
6. The method according to any one of claims 1-5 wherein the residual stream is recycled to the fermentation broth.
7. The method according to claim 6 wherein the hydroxide of the multivalent ion is at least partially deposited.
8. The method according to any one of the previous claims wherein the membrane is an anion-selective membrane.
9. An electrodialysis or electrolysis apparatus for separating a fermentation broth into a residual stream

comprising multivalent ions and lactate ions, comprising a first compartment which is limited by an anion-selective or non-selective membrane, preferably an anion-selective membrane, and a cathode, which further comprises means for introducing the fermentation broth, and a second compartment limited by the anion-selective or non-selective membrane and an anode, which further comprises means for removing lactic acid, and optionally means to recycle the residual stream to the fermentation broth.

10. The electrodialysis or electrolysis apparatus of claim 9 wherein the first compartment further comprises a second membrane being an anion-selective membrane, a non-selective membrane, or a bipolar membrane having its cation-selective side directed to the cathode.

11. The electrodialysis or electrolysis apparatus of claim 9 or 10 wherein the first compartment comprises alternating anion-selective or non-selective membranes and bipolar membranes having their cation-selective sides directed to the cathode.

EPO - DG 1

28. 10. 2002

(43)

Abstract

The invention pertains to a method of separating multivalent ions and lactate ions from a fermentation broth comprising a multivalent ion lactate salt by using an electrodialysis or electrolysis apparatus, comprising the steps of introducing the broth wherein the multivalent ion concentration is at least 0.1 mole/l, the lactate ion concentration is less than 300 g/l, and less than 10 mole% of the lactate ion are other negatively charged ions, into a first compartment of the electrodialysis or electrolysis apparatus, which compartment is limited by an anion-selective or non-selective membrane and a cathode, and wherein the multivalent ion is converted to obtain a residual stream comprising the hydroxide of the multivalent ion, and the lactate ion is transported through the anion-selective or non-selective membrane into a second compartment limited by the anion-selective or non-selective membrane and an anode, after which the lactate ion is neutralized to lactic acid.

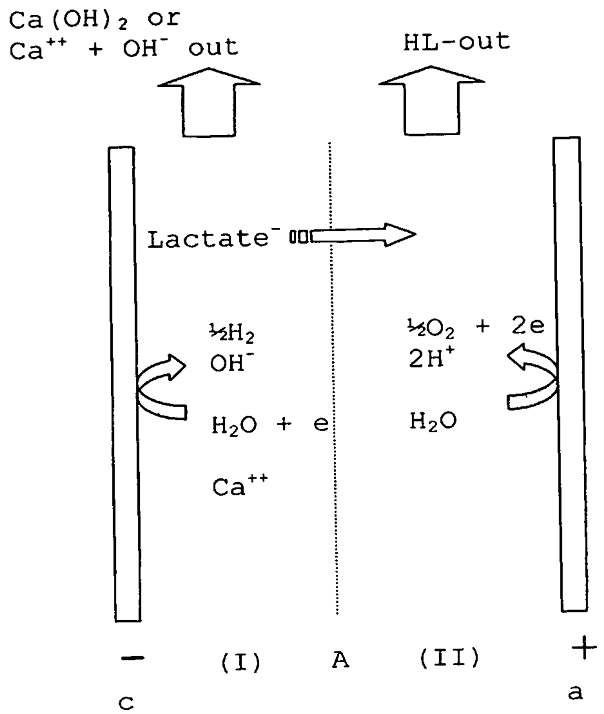
$Ca(OH)_2$ or
Ca^{++} + OH^- out
HL-out
Lactate$^-$
½H_2
OH^-
H_2O + e
Ca^{++}
½O_2 + 2e
$2H^+$
H_2O
−
(I)
A
(II)
+
c
a

Fig. 1

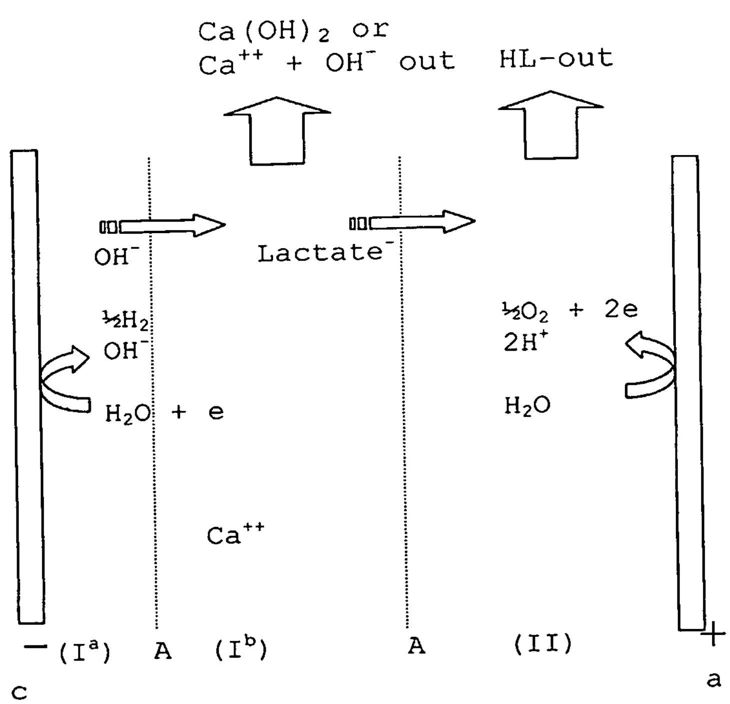
$Ca(OH)_2$ or
Ca^{++} + OH^- out
HL-out
OH^-
Lactate$^-$
½H_2
OH^-
H_2O + e
½O_2 + 2e
$2H^+$
H_2O
Ca^{++}
− (I^a) A (I^b) A (II) +
c
a

Fig. 2

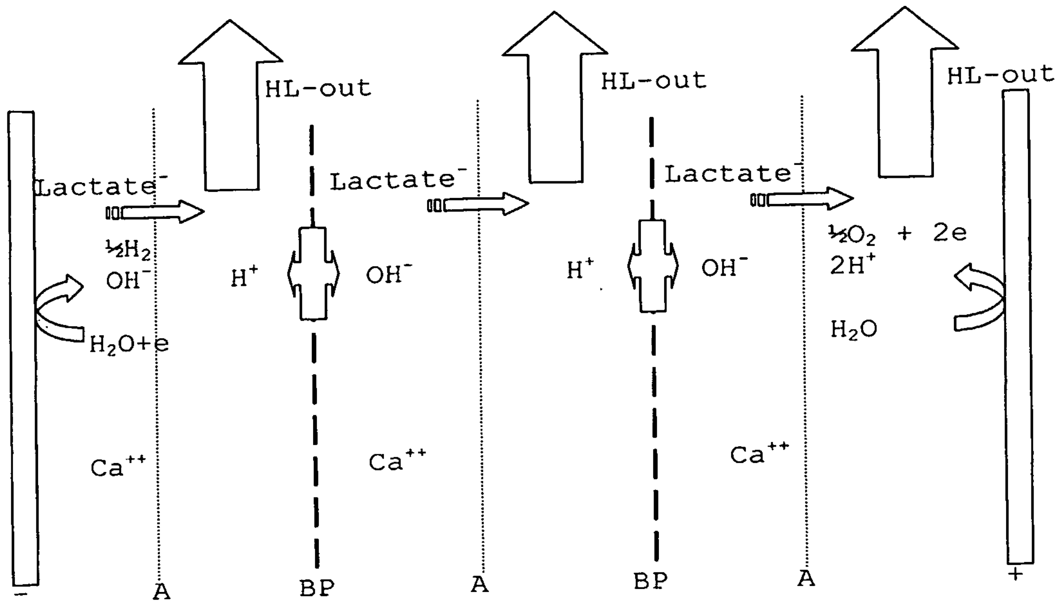
HL-out
HL-out
HL-out
Lactate⁻
Lactate⁻
Lactate⁻
½H2
OH⁻
H2O+e
H⁺
OH⁻
H⁺
OH⁻
½O2 + 2e
2H⁺
H2O
Ca⁺⁺
Ca⁺⁺
Ca⁺⁺
−
A
BP
A
BP
A
+

Fig. 3

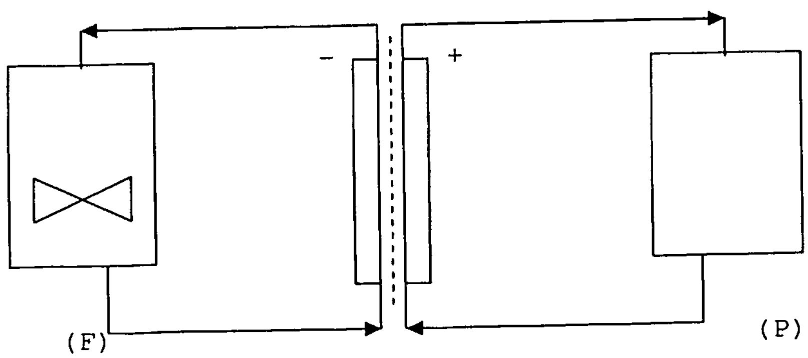
−
+
(F)
(P)

Fig. 4